REMARKS

The Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

I. Status of the Specification & Claims

An updated sequence listing is submitted herewith to correct for minor informalities and alleged misrepresentation, and the Specification as-filed is requested to be amended accordingly to reflect the new sequence listing. In view of the foregoing amendments, the Applicants respectfully submit that the objection to the Specification and sequence listing should now be moot.

Claims 1-22 are cancelled, and new claims 23-44 are added. Claim 23 is added from combining claim 1 with claims 4 and 5. Claim 24 corresponds to claim 14 as filed. Support for claim 25 can be found in, *inter alia,* paragraph [0151] on page 77 of the Specification. Support for claims 26 ad 27 can be found in, *inter alia,* original claim 6 and paragraph [0045] of the Specification. Support for claims 28 and 29 can be found in, *inter alia,* original claim 7. Support for claims 30 ad 31 can be found in, *inter alia,* original claim 8. Support for claims 32 and 33 can be found in, *inter alia,* original claim 9. Support for claims 34 and 35 can be found in, *inter alia,* original claim 10. Support for claims 36 and 37 can be found in, *inter alia,* original claim 11. Support for claim 38 can be found in, *inter alia*, original claim 16, (1) and (3). Support for claims 39-41 can be found in, *inter alia,* original claim 21. Support for claims 42-44 can be found in, *inter alia,* original claim 22. Claims 1-22 are herein cancelled, and the Applicants respectfully reserve the right to pursue the subject matter of the cancelled claims in a subsequent continuation and/or divisional application. No new matter is introduced, and claims 23-44 are currently pending to be examined on their merits.

The Applicants note that in claim 23, SEQ ID NO: 99 corresponds to the amino acid sequence of SEQ ID NO: 30, and SEQ ID NO: 106 corresponds to the amino acid sequence of SEQ ID NO: 57. Also, in claim 38, SEQ ID NO: 110 corresponds to the amino acid sequence of SEQ ID NO: 73 (MABL-2 antibody HL5), and SEQ ID NO: 113 corresponds to the amino acid sequence of SEQ ID NO: 78 (sc(Fv)2 of MABL-2 antibody). The Applicants

further note that all the pending claims read on the elected species. For example, claim 24, corresponding to original claim 14, reads on the elected CDR1, CDR2, and CDR3.

II. Claim Rejections – 35 U.S.C. § 112

Claims 1-9, 12-13, 16, and 21-22 are rejected under 35 U.S.C. §112, ¶2, as allegedly being indefinite. Also, claims 1-9, 12-13, 16, and 21-22 are rejected under 35 U.S.C. §112, ¶1, as allegedly lacking enablement. The Applicants respectfully traverse these rejections.

While not acquiescing to the grounds of the rejections, the original claims are cancelled and new claims 23-44 are added. Specifically, new claims 26 and 27, corresponding to original claim 6, now recite that the humanized antibody of claims 23 and 24, respectively, is a small antibody fragment containing an antigen-binding domain. Also, new claims 42-44, corresponding to original claim 22, no longer recite "(Hodgkin's disease, non-Hodgkin's lymphoma)." Finally, because the new claims recite specific CDRs and FRs of both heavy and light chains that are fully described in the present Specification, the Applicants respectfully submit the present claimed antibodies are fully enabled by the disclosure of the present Specification to reach the presently claimed humanized antibody. The Applicants further note that, as the Office points out on pages 4-6 in the Official Action, several amino acids of the FR are indeed important for antigen binding.

Therefore, at least in view of the foregoing, the Applicants respectfully submit that all of the rejections should now be moot and thus respectfully request that the rejections be withdrawn.

II. Claim Rejections – 35 U.S.C. § 102

Claims 1-4, 6, and 21-22 are rejected under 35 U.S.C. §102(b), as allegedly being anticipated by US 20030108546 ("Fukushima 1"). Claims 1-4, 6-9, and 21-22 are rejected under 35 U.S.C. §02(b)/(e), as allegedly being anticipated by WO 0233073/US 20040242847 ("Fukushima 2"). The Applicants respectfully traverse the rejections.

The present claims are related to humanized anti-CD47 antibodies that comprise specific CDR and FR sequences and have a binding inhibitory activity comparable to or

higher than the parent antibody. Neither Fukushima 1 nor Fukushima 2 discloses the specific antibody sequences, as recited in the present claims. Because neither of Fukushima 1 and Fukushima 2 teaches each and every element as recited in the present claims, neither can anticipate the present claims.

Therefore, at least in view of the foregoing, the Applicants respectfully request that the rejections be withdrawn.

III. Claim Rejections – 35 U.S.C. § 103

Claims 1-9, 12-13, 16 and 21-22 are rejected under 35 U.S.C. §03(a), as allegedly being unpatentable over Fukushima 1, Fukushima 2, each in view of Sato et al. *Cancer Research* 53:851-856, 1993 ("Sato"). The Applicants respectfully traverse the rejections.

(i) Current Obviousness Standard

The U.S. Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a) and held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed and specifically stated:

> Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason to combine the known***

> ***elements in the fashion claimed*** by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex Inc., slip op. at 14 (emphasis added). As discussed below, the cited art cannot render the claimed invention obvious.

(ii) *Fukushima 1 or Fukushima 2, each in view of Sato, does not render the present claims obvious*

As explained in the previous section, neither Fukushima 1 nor Fukushima 2 teaches or suggests the antibody sequences recited in the present claims. Sato does not cure the above deficiencies. Namely, Sato does not teach every element recited in the present claims; and specifically, Sato teaches different FRs from those recited in the present claims. Thus, one of ordinary skill in the art would not have a reason to combine the teaching of either Fukushima 1 or Fukushima 2 with that of Sato. *See KSR Int'l Co.* In fact, even assuming, *arguendo*, these teachings were combined, the presently claimed humanized anti-CD47 antibodies that comprise the specific CDR and FR sequences as recited in the present claims would not result. Thus, the teachings of Fukushima 1, Fukushima 2, and Sato, alone or in combination, do not render the presently claimed antibodies obvious.

Therefore, at least in view of the foregoing, the Applicants respectfully request that the rejections be withdrawn.

CONCLUSION

The Applicants believe that the present application is now in condition for allowance and thus respectfully request favorable reconsideration of the application.

The Office is invited to contact the undersigned by telephone if a telephone interview would advance the prosecution of the present application.

The Office is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, the Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 24, 2009

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